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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,277	08/20/2001	Peter Jozef Leo Hespel	702-010802	6608

7590 08/19/2003

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EXAMINER
GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/19/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/856,277	Applicant(s) HESPEL, PETER JOZEF LEO	
	Examiner Sharmila S. Gollamudi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-18,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-18,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Request for Continued Examination received on June 13, 2003 is acknowledged. Claims 13-18 and 21-22 are pending in this application. Claims 1-12 and 19-20 stand cancelled.

Response to Arguments

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection. In regards to the new and unexpected results, it is pointed out that unexpected results argued by the applicant and the articles cited, have not been provided by the applicant. Upon submission of the articles the unexpected data will be considered. Second, it is pointed out that unexpected results that are not included in applicant's specification should be submitted in a Rule 132 declaration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-18 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of muscle disuse syndrome, does not reasonably provide enablement for prevention of muscle disuse syndrome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: nature of the invention, breadth of the claims, state of the art, guidance of the specification, predictability if the art, and the working examples. All the factors have been considered with regard to the claim, with the most relevant factors discussed below.

Nature of the Invention: The rejected claim is drawn to the method of preventing or treating muscle disuse syndrome in a subject with the administration of the instant compound. The nature of the invention encompasses anticipating the onset of the syndrome and subsequently administering instant composition such that the subject does not manifest any symptoms of muscle disuse.

Breadth of Claims: The complex nature of the claims is greatly exacerbated by the breadth of the claims. The claim encompasses prevention of a syndrome that has many potential causes such as aging, disease, physical handicaps, etc. In order to prevent muscle disuse syndrome completely, one would have to anticipate and envision every possible cause for the syndrome. This may or may not be addressed by the administration of the composition.

Guidance of the Specification: The guidance provided by the specification is geared towards treating at risk patients or those suffering from the symptoms. Therefore in order to diagnose the syndrome, a patient must show signs of the symptom, thus the syndrome is not prevented but rather would be treated by the administration of the composition.

The Amount of Experimentation Necessary: In order to practice the claimed invention, one of ordinary skill in the art would have to first to anticipate the onset of muscle disuse syndrome, the cause of the syndrome, the effective dosage, duration of treatment, etc., to determine whether or not the instant composition prevents the disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art, one of ordinary skill in the art would have to either envision a modification of the variable factors or envision an entirely new combination of the factors, and test the invention again. If unsuccessful again, the whole process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention.

For these reasons the claim is rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 15-18, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Elgebaly (5,091,404).

Elgebaly teach a method of restoring functionality in muscle tissue by administering cyclocreatine. See abstract. Elgebaly discloses that it is known that creatine supplement is effective if it is provided at least two days, especially ten to fourteen days, prior to ischemia. Elgebaly teaches the supplement before and after

ischemia to effect the prompt recover tissue function. See column 1, lines 17-50. Example 1 discloses 120 ml of 5% cyclocreatine prior to surgery and 50 ml every 30 minutes during ischemia and after ischemia. Dosage is 8-12 grams per 70 kilograms.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-18 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pischel et al (5,863,939) in view of Howard et al (5,968,544).

Pischel et al teach a method of administering creatine ascorbates for enhancing muscular development, as a prophylactic against and treatment for ischemia and muscular atrophy. See abstract. The dosage form may be as an oral supplement or intravenous. See column 1, line 56.

Pischel et al do not specify the dosage wherein the amount of creatine is decreased upon treatment.

Howard et al teach a composition containing creatine. The reference discloses that 20-30 grams creatine per day for several days can lead to a greater than 20% increase in human skeletal muscle. Howard discloses that after several days of 20 grams of creatine supplementation, it takes no more than 2 to 3 grams per day to maintain the saturation of body stores. See column 1, lines 40-50 and column 3, lines 10-20. Howard teaches dividing the dose during the day.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Pischel et al and Howard et al and utilize a high creatine loading, followed by a decrease dosage phase. One would be motivated to look to the teachings of Howard et al since Howard teaches the general principle of creatine supplementation and its subsequent utilization in the body. Howard discloses that an increased loading of creatine for several days increases skeletal muscle and creatine saturation is attained. The creatine supply in the body is maintained with a lower dosage. Therefore from Howard's teachings, it is deemed obvious to a skilled artisan that once saturation of a substance is attained in the body, the excess is excreted; thus maintaining the same dosage once saturation has been reached is useless. Further motivation is that Howard discloses that during the high loading phase, increase in skeletal muscles and strength is observed. Therefore since muscle atrophy is characterized by decreasing strength and size of muscles after inactivity, one would be motivated to use Howard's creatine dosage with a reasonable expectation of success of treating Pischel's muscle atrophy.

Claims 13-14, 16-18, and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over XP-00210314 in view of Howard et al (5,968,544).

Wyss et al teach the oral creatine supplementation in muscle disease such as Duchenne and Becker muscular dystrophy, spinal muscular atrophy, etc. See page 334. Wyss discloses that in various muscle diseases the intracellular concentration of creatine and phosphocreatine decreases. See page 334. Wyss teaches two creatine supplement approaches. One being a continuous supplementation of creatine and the other being intermittent short-period supplementation with high doses of creatine. Wyss teaches that the intermittent dosage is favorable since extra creatine can be taken into the muscle cells, which is followed by discontinuing in order to allow recovery of the creatine transporter activity. Wyss teaches an experiment wherein an oral creatine supplement was given to a DMD patient for 155 days. See page 335.

Wyss does not specify the creatine dose.

Howard et al teach a composition containing creatine. The reference discloses that 20-30 grams creatine per day for several days can lead to a greater than 20% increase in human skeletal muscle. Howard discloses that after several days of 20 grams of creatine supplementation, it takes no more than 2 to 3 grams per day to maintain the saturation of body stores. See column 1, lines 40-50 and column 3, lines 10-20. Howard teaches dividing the dose during the day.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wyss et al and Howard et al and utilize a high creatine loading, followed by a decrease dosage phase. One would be motivated

to look to the teachings of Howard et al since Howard teaches the general principle of creatine supplementation and its subsequent utilization in the body. Howard discloses that an increased loading of creatine for several days increases skeletal muscle and creatine saturation is attained. The creatine supply in the body is maintained with a lower dosage. Further motivation is that Howard discloses that during the high loading phase, increase in skeletal muscles and strength is observed. Therefore since muscle disease is characterized by decreasing strength and size of muscles after inactivity, one would be motivated to use Howard's creatine dosage with a reasonable expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG

August 13, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER